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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,709	07/12/2001	Karine Vidal	113308-002	4054

29157 7590 06/06/2005

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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,709	VIDAL ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20-22 and 24* is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,20-22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1a. Receipt of Applicants' amendment and arguments, filed on 25 February 2005 is acknowledged. Claim 18, 20-22 and 24 have been amended. Claims 1-18, 20-22 and 24 are pending, of which claims 1-17 stand withdrawn as they are drawn to non-elected inventions. Claims 19 and 23 have been cancelled. Thus claims 18, 20-22 and 24 are under consideration.

1b. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The following previous objections and rejections are withdrawn in light of Applicants amendment filed 02/25/05.

(I) The rejection of claims 18 and 24 made under 35 USC § 112, second paragraph, for reciting "...the bioactivity of CD14.." and "GI tract..", is withdrawn, because said limitations are no longer recited in these claims. Also claim 22, now recites "70%" instead of "0%".

(II) The rejection of claim 18 under 35 U.S.C § 102(b) as being anticipated by Haziot et al (1995), is withdrawn, because the Haziot et al reference does not teach oral administration of CD14.

(III) The rejection of claims 18, 20-22 and 24 are rejected under 35 U.S.C § 102(b) as being anticipated by Julius et al (1998), is withdrawn, because Julius et al reference does not teach that a CD14 variant can be utilized in treatment or prevention of a gastrointestinal disorder.

Information Disclosure Statements:

3. The information disclosure statement form (PTO 1449) submitted on 17 April 2001 is missing. Please provide this form, so that it can be signed.

Response to Applicants' arguments:

Claim Rejections under 35 U.S.C. §112:

4a. Claims 18, 20-22, 24 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirements, for reasons of record set forth in the office actions mailed on 30 May 2004 and 19 October 2004.

Applicants argue that the GI tract disorders recited in the specification can be treated or prevented by effective mediation of lipopolysaccharide interaction with the gastrointestinal tract. Applicants contend that any factor that is capable of modulating responses to bacteria or their components, such as LPS may be used in the prevention and/or treatment of these disorders. Applicants also submit that claims 21 and 22 are now clarified that the CD14 variant or fragment thereof is at least 70% homologous with the amino acid sequence of human serum CD14 and that it includes SEQ ID NO:1 and that it does not include o-glycosyaltion. Thus applicants conclude that claims 18, 20-22 and 24 now satisfy 35 U.S.C. §112, first and second paragraphs.

These arguments have been fully considered, but are not deemed persuasive. Firstly, it is well known in the art that membrane bound CD14 antigen serves as a high affinity LPS receptor on the surface of monocytes, and that LPS stimulates the release of proinflammatory cytokines such as TNF-α, IL-1, IL-8 and IL-6. It is also well known that a soluble form of CD14 (sCD14) which also binds to LPS significantly improved the outcome of shock in mice challenged with a high dose of LPS, (see Stelter et al,

European Journal of Clinical Investigation, 1998. Vol.28, pages 205-213, especially page 211, see on the 1449 form submitted on 17 April 2001). Thus it is not disputed that the soluble form of CD14 can be used in a method of treating LPS mediated conditions. However, the instant specification does not disclose the structure of a variant of CD14 that lacks O-glycosylation, nor does it demonstrate that said variant of CD14 treats or prevents "all possible" disorders of the gastrointestinal tract of a mammal. Furthermore, the argument that the variant of the instant invention is at least 70% homologous with the serum CD14 that includes SEQ ID NO:1 and that it does not include O-glycosylation, is not found persuasive, because the only description provided for the CD14 variant of the instant invention is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure of CD14 molecule that must be conserved. Nor does it disclose which 106 amino acid residues of the 356 amino acid residues of the mature CD14 polypeptide is altered or deleted. Regarding the limitation that the CD14 variant of the instant invention does not include O-glycosylation, prior art recognizes that the mature CD14 has four potential N-linked glycosyaltion sites (Asn18, Asn132, Asn263 and Asn304), (see Stelter et al, European Journal of Biochemistry, vol.236, 1996, pages 457-464, especially page 457, column 2, this reference is cited on the 1449 form submitted on 30 May 2003). Although CD14 polypeptide might also have O-linked glycosyaltion sites, prior art does not disclose where these sites are located. Moreover, the instant specification does not describe exactly how many O-linked glycosyaltion sites are lacking and where are they located. Accordingly, in the absence of sufficient description

of distinguishing identifying characteristics, the specification does not provide adequate written description of the CD14 variant of the instant invention.

Regarding, "prevention" recited in the claims, Applicants have not disclosed that they were able to determine in advance which mammals were susceptible to a LPS induced gastrointestinal tract disorder, then administer CD14, to prevent said mammal from suffering any gastrointestinal tract disorder.

Therefore, instant specification is only enabling for a method of treating against intestinal bacterial infection by administering soluble CD14.

New Rejections:

Claim rejections-35 USC § 102(b):

5. Claims 18, 20-22 and 24 are rejected under 35 U.S.C § 102(b) as being anticipated by WO 99/61468 (12/1999); This reference is cited on the PTO1449 submitted on 04 August 2003, by Applicant.

5a. WO 99/61468 discloses a method for the prophylactic treatment of a lipopolysaccharide (LPS) induced host inflammatory response in a mammal by administering a therapeutically effective amount of a protein that has at least 63-98% amino acid sequence identity to SEQ ID NO:5, (see bottom of page 7, page 8, lines 1-6). The preferred mode of administration disclosed in the WO 99/61468 patent is by oral administration such that gastrointestinal tract is exposed to the CD14 upon swallowing, (see page 28, fifth paragraph). SEQ ID NO:5 disclosed in WO 99/61468 patent is the mature form of CD14 and it shares 100% homology to SEQ ID NO:1, recited in instant claims 21 and 22. The WO 99/61468 also discloses a method of

ameliorating sepsis comprising administering to a mammal in need thereof an effective amount of a soluble CD14, (see bottom of page 7). The WO 99/61468 patent describes a soluble form of CD14 as lacking glycosylphosphatidylinositol anchor, (see page 3). Thus, the WO 99/61468 patent discloses a CD14 variant that has a different glycosylation pattern than the mature form. Finally, the WO 99/61468 patent discloses that the CD14 can be formulated in an infant formula and be administered to an infant, (see page 27, second paragraph).

Instant claims 18, 21-22 and 24 are drawn to a method of treatment or prevention of a disorder of the gastrointestinal tract of a mammal by administering orally a variant of CD14 or fragment thereof having no O-glycosylation, claim 20 adds the limitation that the variant CD14 is in an infant formula, and claims 21 and 22 further limit the invention the use of a CD14 that shares 70% homology to the SEQ ID NO:1, while claim 24 adds the limitation of administering to "an infant".

The WO 99/61468 patent meets all the limitations recited in instant claims 18, 22-22 and 24.

Claim rejections-35 USC § 112, second paragraph:

6. Claims 18, 20-22 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claim 18 recites "....by mediation of lipopolysaccharide interaction with the gastrointestinal tract.....", however, it is unclear how this mediation is accomplished. It is unclear whether the administration of the CD14 variant inhibits LPS activities, whether

it enhances LPS activities or whether the physical interaction of LPS with the gastrointestinal tract is actually intervened, and if so how?

6b. Claims 21 and 22, still recite the phrase " includes" , which renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. Furthermore, it is unclear what else does the recited serum CD14 comprise, besides SEQ ID NO:1. See MPEP § 2173.05(d).

Conclusion:

7. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
24 May 2005

JANET ANDRES
PRIMARY EXAMINER